REMARKS/ARGUMENTS

Applicants note with appreciation that the Examiner has reconsidered the restriction requirement and decided to rejoin the claims and examine them together. Accordingly, claims 1-40 are currently pending.

In the instant Response, Applicants delete claims 1-9, without prejudice; amend claims 10, 13, 14, 17, 18, 24, 27, 28, 31, 32, 35-40; and add new claims 41-58. Support for amended and new claims drawn to treating individuals with impaired glucose tolerance who have not been diagnosed with NIDDM can be found in the specification in general, and in particular at least at page 3, lines 3-10, where the specification states the need for a therapy to treat IGT, while acknowledging that studies exist for the application of GLP-1 in cases of NIDDM. Thus, in one aspect, the claimed invention is drawn to treating people with IGT who have not been diagnosed with NIDDM.

Claims 13, 14, 27, and 28 have been amended to address the objection to the form of the sequence identifier raised in the Office Action. Claims 17 and 31 have been amended to correct an inadvertent omission. Claims 18 and 32 have been amended to correct a typographical error. Claim 24 has been amended to change the claim from an independent to a dependent claim to accommodate new independent claim 55. Moreover, claim 24 has also been amended to recite the amount of the compound is effective to retard or arrest the loss of plasma glucose control or the development of non-insulin dependent diabetes mellitus (NIDDM), as one of skill in the art would understand from reading the specification would understand the loss of plasma glucose control would not necessarily lead to NIDDM. For example, page 2, lines 2-3, where the specification states that in many, but not all, cases advanced IGT leads to NIDDM. Claim 35 has been amended to change the claim from an independent to a dependent claim to accommodate new independent claim 57 and to correct a typographic error. Claims 36-38 have been amended to more particularly describe the claimed invention, support for which is provided above.

Claims 39 and 40 have been amended to more particularly describe the claimed invention. Support for the claimed invention can be found at least at page 4, lines 9-10, of the specification. Support for new claims 41-43 can be found throughout the specification and in claims 10, 39, and 40, respectively, as originally filed.

Support for new claims 44-58 directed to methods involving exendin and variants thereof can be found in the specification in general, and in particular, at least at Table 1 on page 10, to page 11, lines 11; and page 13, lines 22-23. Accordingly, Applicants submit that no new matter has been introduced by the instant amendments.

Issues concerning the Objection to the Specification and Claims

The Patent Office has objected to the use of "(SEQ. ID NO:__)" as the format identifying a sequence. Applicants have amended the specification and claims to recite to "SEQ ID NO:__" as required by the Patent Office to obviate this objection.

Issues concerning 35 U.S.C. §112, second paragraph

Claims 1-9, 17, and 31 are rejected under 35 U.S.C. 112, second paragraph for allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 is alleged to be indefinite in the recitation of the acronym "GLP-1." Applicants have canceled claim 1, thus obviating this rejection.

Claims 9, 17, and 31 are indefinite in the recitation "having a molecular weight of not greater than about 5000." Applicants have amended the pending claims to reference the correct unit of measurement of the compound, *i.e.*, 5000 daltons, to overcome this portion of the rejection. As for the use of "about," Applicants submit that under the guidance of MPEP 2173.05(b), the tem "about," as used in the instant application, would be sufficiently clear to one of ordinary skill in the art. "About" is an art-recognized term and is appropriate under these circumstances, as one of skill in the art knows that many

techniques for measuring molecular weight do not yield a precise number. For example, proteins can be measured on an SDS page gel in relation to a standard molecular weight marker; however, there are gaps between markers where one has to estimate the size. Moreover, as the Patent Office itself acknowledges, molecular weights might vary slightly depending on the technique used. Thus, Applicants submit that the use of "about" in the context of describing a compound's molecular weight is appropriate and would allow those of skill in the art to understand the scope of the claimed invention. Accordingly, Applicants request reconsideration and withdrawal of the rejection under 35 U.S.C. 112, second paragraph to pending claims 17 and 31.

Issues under 35 U.S.C. §102(b)

Claims 1-8 and 39-40 are rejected under 35 U.S.C. 102(b) for allegedly being anticipated by WO 98/08531. Applicants respectfully traverse this rejection.

Claims 1-8 have been canceled, rendering the rejection moot as to these claims. Claims 39-40 have been amended to more particularly describe the claimed invention. Claims 39 and 40 are directed to methods of reducing the risk of cardiovascular and cerebrovascular events, respectively.

Reference WO 98/08531 discloses the use of GLP-1 or analogs to treat myocardial infarctions in patients incapable of autoregulation of blood glucose (the reference in general, page 19, line 30 to page 20, line 2 in particular) by normalizing blood glucose. Applicants submit that reference WO 98/08531does not teach methods for reducing the risk of cardiovascular or cerebrovascular events as set forth in amended claims 39 and 40. Accordingly, Applicants respectfully request reconsideration and withdrawal of the rejection of claims 39 and 40 under 35 U.S.C. 102(b) based upon reference WO 98/08531.

Issues under 35 U.S.C. §103(a)

Claims 1-40 have been rejected under 35 U.S.C. 103(a) for allegedly being unpatentable over reference WO 98/08531 taken with Rachman *et al.* (Diabetologia, Vol. 40, pp. 205-211, 1997) (hereinafter referred to as "Rachman"). Applicants respectfully traverse this rejection.

Claims 1-9 have been canceled, thus rendering this rejection moot as to those claims. Claims 10-38 have been amended to recite to the treatment of IGT in a patient who has not been diagnosed with non-insulin dependent diabetes mellitus (NIDDM). Claims 39 and 40 have been amended to recite to a method of reducing the risk of a cardiovascular or cerebrovascular event.

Reference WO 98/08531, as previously discussed, discloses treating acute myocardial infarctions in people who are incapable of autoregulation of blood glucose by normalizing blood glucose levels. Reference WO 98/08531 does not teach treating IGT, as recognized by the Patent Office on page 8, lines 23-25, of the Office Action. For that matter, reference WO 98/08531 does not even teach treating NIDDM, as recognized by the Patent Office on page 8, lines 14-17, of the Office Action, "[t]he reference is mainly directed to a method of reducing mortality and morbidity after myocardial infarction by administering GLP-1 and a GLP-1 analog or derivative thereof at a dose effective to normalize blood glucose."

Rachman is cited to cure the defect of reference WO 98/08531. Rachman is alleged to disclose that "continuous infusion of GLP-1 markedly improved both overnight and daytime glucose concentrations in subjects with NIDDM reduced plasma glucose concentrations and stimulated insulin secretion in IGT and NIDDM subjects, wherein GLP-1 restored the ability of β-cell to sense and respond to plasma glucose in all IGT subjects with a variable response who had already developed NIDDM." (See page 9, lines 9-13 of the Office Action.)

Applicants respectfully submit, however, that Rachman only studied the effect of continuous administration of GLP-1 in subjects with NIDDM and used non-diabetic subjects as the control. For example, on page 206, under the section entitled "Subjects and methods," eight patients with NIDDM and six non-diabetic control subjects were used. The non-diabetic control subjects are all reported to have normal fasting glucose values and normal glucose responses to a standard meal-tolerance test. Accordingly, Rachman does not contemplate use of GLP-1 on IGT subjects, only NIDDM subjects.

Moreover, on page 209, second column, lines 24-30, of Rachman, it states that "[a]lthough GLP-1 markedly improved the impaired basal beta-cell function of subjects with NIDDM, the impaired postprandial beta-cell function was only slightly improved, suggesting that there were defects in control of postprandial insulin secretion in NIDDM for which GLP-1 does not compensate." Again, Rachman only contemplates the effect of GLP-1 on NIDDM. Furthermore, Rachman suggests that, based on the study, GLP-1 does not restore the ability of β-cells to sense and respond to plasma glucose (*e.g.*, the postprandial rise in blood glucose in response to a meal) in NIDDM.

Accordingly, neither reference WO 98//08531 nor Rachman, alone or in proper combination, teach each and every limitation of the claimed invention. Neither teaches or suggests that GLP-1 can be used to treat IGT or reduce the risk of a cardiovascular or cerebrovascular event as set forth in claims 10-40.

For the reasons set forth above, Applicants respectfully request reconsideration and withdrawal of the rejection of the pending claims 10-40 under 35 U.S.C. 103(a) based upon WO 98/08531 in view of Rachman.

Citation of Relevant Prior Art

Applicants note that the Patent Office considers the prior art U.S. Patent 6,344,180 to Holst, of record and not relied upon, to be pertinent to Applicants' disclosure. Applicants respectfully wish to state for the record that they do not concede

that Holst is a proper prior art reference based upon a cursory review of the priority information.

CONCLUSION

Applicants respectfully submit that the claims are now in condition for allowance and request that a timely Notice of Allowance be issued in this case. The Examiner is encouraged to call the undersigned attorney to discuss any issues related to the prosecution of the instant application.

Applicants believe that no additional fee is necessitated by the instant paper. However, in the event any additional fees are due or any amount is to be credited, Applicants authorize the Commissioner of Patents to debit or credit Deposit Account No. 010535.

Respectfully submitted,

Mi K. Kim
Reg. No. 44,830

AMYLIN PHARMACEUTICALS, INC.
9360 Towne Centre Drive
Suite 110
San Diego, CA 92121
Phone: (858) 552-2200
Facsimile: (858) 552-1936